# High-fidelity Computational Simulation to Refine Strategies for Lung-Protective Ventilation in Paediatric Acute Respiratory Distress Syndrome

**Short Title:** Strategies for protective ventilation in paediatric ARDS

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**Funding:** DGB and JGH acknowledge funding from the UK Engineering and Physical Sciences Research Council (Grant No. EP/P023444/1). NY acknowledges funding from the NIH (Grant No. NIH K23 HL-136688).

**Keywords:** Paediatric ARDS; Mechanical ventilation; Ventilator-induced lung injury; Protective ventilation; Paediatric intensive care; Computer simulation.

**Article Tweet**: Analysis of a new patient dataset suggests strategies for achieving more protective mechanical ventilation of paediatric ARDS patients.

**Take-home message**: PARDS patients may be being routinely over-ventilated. We have developed and tested novel algorithms for reducing damaging ventilator pressures and tidal volumes in PARDS subjects.

**Conflict of Interest:** The authors declare that they have no conflicts of interests.

To the editor:

Mechanical ventilation in paediatric acute respiratory distress syndrome (PARDS) is less studied than in adults, with guidelines for ventilation adapted from adult ARDS. However, PARDS has a distinct epidemiology, and adult ARDS guidelines may not be appropriate in children. As an example, clinical trials suggest that lower tidal volumes ($V_T$) reduce mortality in adult ARDS [1]. Recent research has also highlighted the potential of lung-protective strategies based on limiting driving pressure ($\Delta P$) and mechanical power to reduce ventilator induced lung injury (VILI) [2, 3]. However, no trials have tested protective ventilation in PARDS, observational studies are unclear [4], and concerns about hypercapnia or increased dead space in paediatrics contribute to hesitancy to lower $V_T$. There is thus an urgent need for studies that can provide additional evidence regarding how lung-protective ventilation could be implemented in PARDS. We hypothesized that analysis of a large PARDS dataset using a computational simulator would allow us to (a) determine the scope (in terms of lowering $V_T$, $\Delta P$, and mechanical power) for safely implementing more protective ventilation; and (b) develop, test, and directly compare strategies for achieving this.

Using a prospective cohort of PARDS from the Children's Hospital of Philadelphia with detailed data collection (see Supplement), we developed and tested four lung-protective strategies for reducing either $V_T$ (strategies 1-3) or $\Delta P$ (strategy 4). Strategy 1 reduced $V_T$ maintaining constant minute ventilation, strategy 2 reduced $V_T$ maintaining alveolar ventilation with a fixed duty cycle, strategy 3 reduced $V_T$ maintaining alveolar ventilation with fixed inspiratory flow, and strategy 4 simultaneously reduced $V_T$ and $\Delta P$. The simulations continued incrementally reducing $V_T$ until safety constraints (hypoxemia, hypercarbia, peak pressure > 35 $cmH_2O$, respiratory rate [RR] > 40 breaths/minute) were violated.

The simulator accurately reproduced patient data (Figures 1 and S2) in a development cohort of 30 patients (aged between 2.5 and 4 years). Similar $V_T$ reductions were achieved using strategies 1 to 3 (15%, 12%, and 14%; Figures S3-4), with the number of patients being ventilated using $V_T > 10$ mL/kg falling to zero. Strategy 1 produced no significant change in mechanical power (+1%; $p = 0.2$, signed-rank test) but both strategies 2 and 3 resulted in increases (+22% and +19%; both $p < 0.05$). Strategy 4 reduced $\Delta P$ -6% for all 30 patients in the cohort, and -17% for the 13 patients on which this strategy could be applied without violating constraints. Strategy 4 was the only approach that produced a significant reduction in mechanical power (-8%; $p < 0.05$). Similar trends were seen in test cohort 1 (ages 1-2 years) and 2 (initial $V_T > 10$ mL/kg), with test cohort 2 showing the greatest potential for lung-protective ventilation (Figures S6-7).

Our data suggests PARDS patients are routinely over-ventilated, and that there is scope for achieving protective ventilation without compromising gas exchange. Such interventions could be readily implemented at the bedside by clinicians directly, or automatically via closed-loop control algorithms. Our results support the design of randomized trials to better delineate the role of lung-protective ventilation in PARDS.

## REFERENCES


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## FIGURE LEGENDS

**Figure 1:** Development Cohort, a comparison of the outputs of the simulator with the original patient data in panels (a) and (b), expressed as median, interquartile range and actual range. Panels (c) to (f) also plot the data points (on horizontal axis) versus simulator output values (on vertical axis). R is the Spearman's rank correlation coefficient.